Decision Memo for Percutaneous Transluminal Angioplasty (PTA) of the Carotid Artery Concurrent with Stenting (CAG-00085N)

Decision Summary

Amend CIM 50-32 to state:

PTA is not covered to treat obstructive lesions of the carotid artery except in the following circumstance:

Medicare will cover PTA of the carotid artery concurrent with stent placement in clinical trials that receive a Category B IDE designation from the FDA. PTA of the carotid artery, when provided solely for the purpose of dilation concurrent with carotid stent placement, is considered to be a reasonable and necessary service only when provided in the context of such a clinical trial, and therefore is considered a covered service for the purposes of these trials. Although the carotid stent used in this procedure is presently under evaluation as a Category B investigational device, the PTA used to place the stent (and all services related to this procedure) are considered covered services.

Performance of PTA in the carotid artery when used to treat obstructive lesions outside of an approved Category B IDE clinical trial remains a noncovered service.

PTA of the of the vertebral and cerebral arteries remains noncovered.

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Decision Memo

TO: Administrative File CAG: #00085N
Percutaneous Transluminal Angioplasty Concurrent with Carotid Artery Stenting

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SUBJECT: National Coverage Decision
DATE: March 19, 2001

This memo serves four purposes: (1) outlines the causes and treatment of carotid artery disease and stroke; (2) reviews the history of Medicare's coverage process on percutaneous transluminal angioplasty (PTA) of the carotid artery and provides a timeline of recent activities related to that decision; (3) presents and analyzes the relevant scientific and clinical data related to PTA concurrent with carotid artery stenting; (4) delineates the reasons for limited coverage of PTA of the carotid artery when provided in the context of an Food and Drug Administration (FDA) approved Category B Investigational Device Exemption (IDE) trial.

Background

Currently, Medicare does not cover PTA to treat obstructive lesions of the carotid, cerebral and vertebral arteries (Coverage Issues Manual (CIM) section 50-32).

In the late 1980s, clinicians began investigating the use of endovascular stents (placed in the carotid artery) for the treatment of carotid stenosis. Several large Category B IDE studies have recently been approved by the FDA or are in the approval process to investigate carotid artery stenting. In general, carotid angioplasty is required to dilate the stenosis during the stent placement procedure. Because of the existing noncoverage policy for PTA of the carotid artery, none of the services related to this angioplasty would be covered by Medicare for beneficiaries participating in these clinical trials, despite the stents' designation as a Category B device.

HCFA recognizes that these clinical trials are designed to evaluate the safety and effectiveness of medical care, and are crucial to potentially improving clinical practice. Accordingly, this decision analyzes whether carotid angioplasty, when performed solely for the purpose of dilation concurrent with carotid stent placement, should be considered a reasonable and necessary service when provided in the context of an approved Category B IDE clinical trial.

History of Medicare's Coverage of PTA and Timeline of Recent Activities

See CIM section 50-32 for Medicare's policy regarding PTA

Currently, PTA is not covered to treat obstructive lesions of the carotid, vertebral, and cerebral arteries. As a result, any services related to PTA of these arteries, including services related to follow-up care and complications which require treatment during the same hospital stay in which the PTA was performed, are not covered services under Medicare.[1]

Since the early 1980s, HCFA has critically examined the scientific and clinical evidence related to PTA of various vessels, and the HCFA Technology Advisory Committee (TAC) and its predecessor, the HCFA Physicians Panel, have both examined this issue. As a result, HCFA coverage policy regarding PTA of various vessels has been continually expanded as the scientific and clinical evidence have validated the effectiveness of this procedure in coronary, peripheral, and renal vessels.

As early as 1980, the HCFA Physicians Panel consensus was that PTA for noncoronary vessels (primarily artherosclerotic lesions of the iliac, popliteal, and femoral arteries) was generally accepted and performed. In 1981, the Panel requested that the National Center for Health Care Technology (NCHCT), the predecessor to the Office of Health Technology Assessment (OHTA), assess the effectiveness of PTA in non-coronary vessels. At that time, there was no HCFA national coverage policy related to non-coronary vessels. As a result, Medicare contractors had discretion in determining coverage for these procedures.

In May 1981, coverage of PTA for the treatment of atherosclerotic obstructions in the lower extremities became effective.

In 1984, HCFA received an OHTA assessment titled "*Percutaneous Transluminal Angioplasty For Obstructive Lesions of the Aortic Arch Vessels*." In this assessment, the OHTA critically evaluated the published literature regarding this procedure. These articles were limited to early case reports where PTA was used to treat stenotic lesions of the carotid arteries.[2] The assessment noted that although these studies reported a high degree of success and low complication rate (when careful selection of patients were made and angioplasty was performed by an experienced individual), the "treatment of patients with obstructive lesions of the aortic arch vessels with PTA is a relatively new procedure that lacks adequate long-term follow-up."

In conclusion, the OHTA assessment recommended that "not until substantially more dilations with PTA have been carried out in carefully performed controlled studies will it be possible to define the safety and clinical effectiveness of the procedure in the carotid, subclavian, and vertebral arteries and compare it to the outcome with conventional surgery."[3]

Upon receipt of this report, HCFA issued a national noncoverage policy for PTA for the treatment of obstructive lesions of the aortic arch vessels. Subsequent to this noncoverage policy, HCFA amended the PTA policy to cover obstructive lesions of a single coronary artery (for certain indications), the upper extremities (not including the head and neck), the renal artery (as an alternative to surgery for certain patients), and arteriovenous dialysis fistulas and grafts when performed through either a venous or arterial approach.[4]

Following a request from a physician for Medicare coverage of PTA for lesions in the subclavian and other non-coronary vascular territories, the TAC reviewed this policy again in February 1993. The TAC examined the current literature and heard testimony from Jacques Theron, MD, a recognized expert in the field of angioplasty of supra-aortic arteries. Dr. Theron noted that PTA of the carotid artery was feasible but that the "true risks and potential benefits have to be investigated further." Furthermore, the TAC noted that several other authors of small studies of PTA of carotid arteries expressed similar concerns.[5] The TAC raised several issues for discussion, including: (1) Is there enough available data to assess the use of PTA in the aortic arch vessels; including the carotid, subclavian, and vertebral arteries; (2) Should Medicare Coverage policy be changed in CIM 50-32 to allow coverage for the use of PTA in these vessels; and, (3) Should there be any specific patient and/or provider criteria included if PTA in these vessels is covered?

At a subsequent meeting in June 1993, the TAC members discussed these issues, as well as additional information they had received from the Society of Cardiovascular and Interventional Radiology (SCVIR). The SCIVR agreed that PTA for upper extremity vessels was an effective and appropriate therapeutic procedure, but that PTA of head and neck vessels remained investigational. The TAC concluded that CIM 50-32 should be revised to allow Medicare coverage of PTA for upper extremity vessels (including the subclavian artery) and the renal artery, but concluded that PTA of vessels for cerebral circulation should remain noncovered.[6] Medicare national coverage policy was revised to reflect these recommendations, and PTA of carotid, vertebral, and cerebral arteries to treat obstructive lesions remained noncovered.

In September 1995, HCFA issued regulations related to Medicare coverage of certain devices with an IDE approved by the FDA.[7] As part of this process, HCFA entered into an interagency agreement with the FDA to identify those investigational devices that are of a device type for which the underlying questions of safety and effectiveness have been resolved. Under this categorization process, the FDA assigns each device with an an FDA -approved IDE to one of two categories: Experimental/Investigational (Category A) Devices, or Non Experimental/Investigational (Category B) Devices. HCFA excludes from Medicare coverage all devices with an IDE that are categorized by the FDA as Category A. However, under this regulation, HCFA permits its Medicare contractors to consider coverage on a local basis for Category B devices that are provided in accordance with an FDA approved trial protocol. These devices (and related services) then may be covered by Medicare if all other applicable coverage requirements are met.

This policy was intended to as provide Medicare beneficiaries with earlier access to the latest advances in medical technology while facilitating the collection of information about these Category B devices through clinical trials.

In 1997, the TAC analyzed the issue of PTA of the carotid artery with stenting. An analysis of the published literature was prepared and presented to the TAC members. This analysis concluded that the small, non-randomized studies describing carotid angioplasty-stenting "lack complete descriptive information and have limited or absent outcomes and follow-up data. As a result, the findings that are reported cannot be generalized to large populations."[8] At that time, several TAC members expressed their belief that current noncoverage policy for PTA of the carotid, vertebral, and cerebral arteries should continue in light of the evidence, but that the best mechanism for compiling clinical data regarding the safety and effectiveness of carotid stenting would be a randomized clinical trial. The TAC was aware of discussions between carotid angioplasty-stenting investigators and the National Institutes of Health (NIH). It was in favor of discussions between these parties and HCFA to support a protocol approved by the NIH, with reimbursement provided by HCFA for those Medicare beneficiaries who participated in the study.

Due to the noncovered status of the angioplasty, the TAC agreed that until a modification of the PTA policy was made, stents used during carotid angioplasty in an FDA approved Category B IDE trial should not be covered.[9] At the time, HCFA had several meetings with proponents of this proposed trial, but no action was undertaken by the agency to amend CIM 50-32.[10]

Timeline of Recent Activities

August 12, 1999	Representatives from the Carotid Revascularization Endarterectomy-Stenting Trial (CREST) executive committee, Guidant, Inc., FDA, HCFA, and the National Institute of Neurological Disorders and Stroke (NINDS) met at HCFA headquarters in Baltimore to discuss the CREST protocol and schedule of enrollment. At this meeting, CREST Principal Investigator Robert Hobson, MD, reiterated that the trial's success in recruiting patients would be dependent on HCFA reimbursement.
October 5, 1999	Grant Bagley, MD, JD, Director of the Coverage and Analysis Group (CAG), received a letter from Mark Wholey, MD, Chairman of the Pittsburgh Vascular Institute and an expert in carotid angioplasty-stenting. Dr. Wholey expressed strong support for reimbursement of this procedure, based on the scientific data.

November 17, 1999	Representatives from Cordis, Inc., Kenneth Ouriel, MD, FACS, the Chaiman of the Department of Vascular Surgery at the Cleveland Clinic, and Jay Yadav, MD, the Director of Interventional Cardiology at the Cleveland Clinic Foundation, met with Jeffrey Kang, MD, MPH, Director of the Office of Clinical Standards and Quality, and CAG staff to discuss carotid artery stenting of high-risk patients and the SAPPHIRE trial.[11] Brian Firth, MD, PhD, Vice President, Medical Affairs & Health Economics Worldwide at Cordis, requested that HCFA provide reimbursement for Medicare patients enrolled in the Stenting and Angioplasty with Protection in Patients at High-Risk for Endarterectomy (SAPPHIRE) trial. However, Cordis did not submit a formal coverage request for this trial.
March 17, 2000	Representatives from Boston Scientific, Inc., as well as L.N. Hopkins, MD, Chairman of Neurosurgery at the State University of New York at Buffalo, met with CAG staff to discuss the medical necessity of carotid stenting for a subset of patients with carotid artery stenosis. Representatives from Boston Scientific, Inc. discussed their plans for a carotid stenting trial for high-risk surgical patients, and asserted that carotid stenting with or without PTA is reasonable and necessary care for a subset of patients with carotid artery stenosis. However, Boston Scientific did not submit a formal coverage request regarding carotid angioplasty-stenting.
April 26, 2000	Hugh Hill, MD, JD, Acting Director of CAG, and CAG staff met at FDA headquarters with representatives from FDA and NINDS to discuss carotid stenting trials.
June 28, 2000	Jeffrey Kang, MD, MPH, received a letter from Gerald Fishbach, MD, Director of NINDS. Dr. Fishbach stated that HCFA support for those Medicare patients enrolled in the CREST trial was an important consideration in NINDS awarding a grant of $23.9 million to the CREST investigators in January 1999.
July 7, 2000	President Clinton issued a memorandum to Health and Human Services Secretary Donna Shalala about increasing participation of Medicare beneficiaries in clinical trials.
July 28, 2000	HCFA Administrator Nancy-Ann Min Deparle received a letter signed by 14 US senators requesting that HCFA reimburse the hospitalization costs of patients participating in the CREST trial.
August 7, 2000	Dr. Robert Hobson met with Sean Tunis, MD, MSc, Director of CAG, regarding the impact of President Clinton's Executive Memorandum on the CREST trial.
September 19, 2000	Medicare clinical trials coverage policy went into effect.
October 11, 2000	Representatives from Boston Scientific, Inc. and CAG held a conference call to discuss HCFA's national noncoverage policy for PTA. The discussion centered around coverage for carotid stenting with distal protection devices within Boston Scientific's proposed clinical trial and the impact of the new clinical trials policy on trials involving PTA of the carotid artery concurrent with stenting.
October 19, 2000	Representatives from Guidant, Inc., and William Gray, Director of the Endovascular Lab at the Swedish Heart Institute, met with members of CAG to discuss carotid angioplasty-stenting. At this meeting, representatives from Guidant, Inc. stated that the national noncoverage decision for carotid PTA should not apply to carotid stenting. Guidant, Inc. did not submit a formal coverage request regarding this issue.
November 22, 2000	Representatives from Cordis, Inc. met with Dr. Tunis and CAG staff to discuss coverage of the SAPPHIRE trial.
December 18, 2000	HCFA internally generated a formal national coverage request for PTA of the carotid artery concurrent with stenting. In the tracking sheet posted on the coverage website regarding this issue, HCFA stated that it is "currently evaluating whether carotid angioplasty, when performed solely for the purpose of pre-dilation concurrent with carotid stent placement, should be considered a reasonable and necessary service when provided in the context of an approved Category B IDE clinical trial."[12]
December 2000-March 2001	HCFA staff reviewed study protocols, published studies, and clinical information related to this topic. In addition, staff spoke with experts on carotid angioplasty-stenting and continued dialogue with interested parties. Letters supporting this issue were received from manufacturers, the American College of Cardiology, and several clinicians.

Clinical Background

The generic term "stroke" signifies the abrupt impairment of brain function caused by a variety of pathologic changes involving one or several intracranial or extracranial blood vessels.[13] In general, stroke is defined as a neurologic deficit lasting more than 24 hours, while a transient ischemic attack (TIA) is typically described as a similar neurologic deficit lasting less than 24 hours. More than 600,000 new and recurrent strokes occur in the US each year, resulting in approximately 160,000 deaths.[14] Stroke is the third leading cause of death in the US behind cardiovascular disease and cancer, and is the leading cause of serious, long-term disability. Approximately 70% of all strokes occur in people age 65 and older.

Risk factors for stroke include genetics, lifestyle choices, and disease processes. Hypertension is the most powerful, prevalent, and treatable risk factor for stroke. Other risk factors include smoking, alcohol use, age, gender, race, diet, blood lipid level, and cardiovascular disease.

Between 70-80% of all strokes are caused by decreased blood flow in an artery supplying blood to the brain (ischemic stroke). The remaining 20-30% are caused by cerebral and subarachnoid hemorrhages (hemorrhagic stroke).[15] Atherosclerosis of extracranial and intracranial arteries accounts for approximately two thirds of all ischemic strokes and an even greater proportion of those affecting patients over the age of 65.[16] Atherosclerosis generally causes stroke either by in situ stenosis or occlusion or by embolization of plaque thrombus material to cerebral vessels. About 20% of all ischemic strokes are due to carotid or cerebral arterial stenosis.[17]

Carotid artery stenosis usually is identified after TIA, but for a significant number of patients, cerebral infarction caused by embolism or carotid occlusion is the primary event.[18] The annual stroke event rate for asymptomatic patients with hemodynamically significant carotid artery stenosis ranges from 2% to 5%.[19]

Prevention of stroke includes treatment of hypertension and diabetes mellitus, smoking cessation, limiting alcohol intake, control of diet and obesity, antiplatelet drugs or anticoagulants for atrial fibrillation and selected acute myocardial infarctions, antiplatelet drugs for symptomatic carotid or vertebrobasilar atherosclerosis, and carotid endarterectomy CEA for defined populations of patients with symptomatic or asymptomatic carotid artery stenosis.

Carotid Endarterectomy (CEA)

CEA is a surgical procedure performed to remove stenotic or ulcerated plaques from affected carotid arteries in order to prevent stroke. The first CEA was performed in the early 1950s, and the number of these procedures performed grew steadily in the US through the 1970s and early 1980s. In the mid 1980s, a number of studies were published which demonstrated very high rates of peri-operative complications after the procedure, thus raising questions about the benefit of CEA in preventing stroke.[20] Coupled with increasing evidence that other, non-invasive therapies were effective in reducing stroke[21], investigators launched several large, randomized, multi-center clinical trials comparing the effectiveness of CEA to medical management.[22]

The European Carotid Surgery Trial (ECST)[23] randomized 2,518 patients with either mild (0-29%), moderate (30-69%) or severe (70-99%) carotid artery stenosis to either immediate surgery or no immediate surgery at 80 European medical centers. Symptomatic patients with 70-99% stenosis (455 surgery vs. 323 no-surgery) were followed for a mean duration of 2.7 years. Exclusion criteria included carotid occlusion, severe intracranial stenosis, cardioembolic stroke, uncontrolled diabetes or hypertension, renal failure, and chronic obstructive pulmonary disease.

During the three-year follow-up period, the risk of ipsilateral stroke and perioperative death was 10.3% for patients who had CEA and 16.8% for patients treated with medical management only ($p<0.0001$). The total risk of surgical death, surgical stroke, ipsilateral stroke, or any other stroke was 12.3% for surgery and 21.9% for non-surgery ($2p<0.01$). No benefit from CEA was found in patients with 0% to 29% stenosis.[24]

The North American Symptomatic Carotid Endarterectomy Trial (NASCET)[25] randomized 328 patients to surgery and 331 patients to medical management at 50 centers in the US and Canada.[26] All enrolled patients had a hemispheric or retinal TIA or a nondisabling stroke within the 120 days prior to entry and had stenosis of 70-99% in the symptomatic carotid artery. Exclusion criteria included carotid occlusion, severe distal internal carotid artery stenosis, cardiac embolism, prior CEA, or medical illness that would preclude a five-year life expectancy.

Thirty-day stroke morbidity and mortality rate for the CEA group was 5.8%, and the cumulative risk of any ipsilateral stroke at two years was 9% for CEA patients versus 26% for medical patients ($p<0.001$).[27] The corresponding estimates for major or fatal ipsilateral stroke were 2.5% versus 13.1% ($p<0.001$), respectively. Subsequent reports from the NASCET investigators concluded that among patients with stenosis of 50-69%, the five- year rate of any ipsilateral stroke was 15.7% among CEA patients and 22.2% among medically treated patients ($p=0.045$). In patients with less than 50% stenosis, the 5-year rate of any ipsilateral stroke was not significantly different (14.9% among CEA patients and 18.7% among medically treated patients, $p=0.16$).[28]

The Veterans Affair Symptomatic Endarterectomy Trial[29] randomized 92 men to CEA and medical management and 101 men to medical management alone at 16 university affiliated Veterans Affairs Medical Centers.[30] All patients had symptoms within 120 days of entering the study, and angiographically determined internal carotid artery stenosis greater than 50% ipsilateral to the presenting symptoms. At a mean follow-up time of 11.9 months, there was a significant reduction in stroke or crescendo TIA in patients who received CEA (7.7%) compared with non-surgical patients (19.4%), or an attributable risk of 0.6 (absolute risk reduction, 11.7%; p=0.011). Among patients with stenosis >70%, the benefit of surgery was more pronounced (7.9% vs 25.6%), with an attributable risk of 0.7 (absolute risk reduction, 17.7%; p=0.004). There was no significant difference in the rates of stroke and death between medical and surgical treatment in men with greater than 50% carotid stenosis who had symptoms of cerebral or retinal ischemia within three months.

The Asymptomatic Carotid Athererosclerosis Study (ACAS)[31] randomized 828 patients to CEA (3 lost to follow-up) and 834 patients to medical management at 39 centers. Unlike the previously cited studies, ACAS investigated whether CEA, when added to aggressive reduction of modifiable risk factors and administration of aspirin, reduced the 5-year risk of ipsilateral stroke in individuals with asymtomatic hemodynamically significant carotid artery stenosis. Although one previously published study reported positive results in patients who had received CEA for asymptomatic carotid artery stenosis[32], ACAS was the first large randomized multi-center trial to investigate CEA in asymptomatic patients.

The ACAS definition of hemodynamically significant carotid stenosis required that at least one of three angiographic or Doppler ultrasound criteria were met. Exclusion criteria were: cerebrovascular events in the study carotid artery or in the vertebrobasilar arterial system; symptoms referable to the contralateral cerebral hemisphere within the previous 45 days; contraindication to aspirin therapy; a disorder that could seriously complicate surgery; or a condition that could prevent continuing participation or was likely to produce disability or death within five years.

Two point three percent of patients who received CEA had a stroke or died during the perioperative period compared to .4% in the medical group. After a median of 2.7 years of follow-up, the estimated five-year risk of ipsilateral stroke and any perioperative stroke or death was 11% for the medical group and 5.1% for the surgical group (p=0.004). The reduction in five-year ipsilateral stroke risk in the surgical group was 53% of the estimated five-year risk in the medical group.

These studies have demonstrated that CEA is an effective procedure to prevent stroke in symptomatic patients with carotid stenosis >70% or more, and for certain asymptomatic patients with carotid stenosis >60% when surgery is performed in high-volume centers by highly proficient surgeons.[33] In patients with or without symptoms who have carotid stenosis <60%, the effectiveness of CEA is not known, and ongoing studies are examining this question. Although concerns about the generalizability of the trials (due to patient selection and other possibly flawed design parameters) has been vigorously debated,[34] CEA has been established as the preferred management for select patients with high-grade symptomatic and asymptomatic carotid stenosis. The number of CEAs performed has steadily grown since 1991, with approximately 140,000 done in the US by the late 1990s,[35] with nearly 70% performed on Medicare patients.

Nevertheless, CEA carries a small but measurable risk of causing death and disabling stroke, with the risk varying somewhat as a function of the skill and experience of the surgeon and the volume of surgeries performed at a particular center. In NASCET, peri-operative mortality in the CEA group was 0.6% compared to 0.3% for the medical management group. Several authors have also noted the increased morbidity and mortality associated with CEA performed in certain high-risk groups. Examples of high- risk patients include those with: (1) severe congestive heart failure; (2) recent myocardial infarction (MI); (3) unstable angina; (4) severe coronary artery disease; and, (5) severe chronic obstructive pulmonary disease.

Ouriel et al. retrospectively analyzed results of CEA performed in 3,061 patients at the Cleveland Clinic over a ten -year period.[36] A high-risk subpopulation was defined as those patients with one or more of following: (1) congestive heart failure; (2) coronary bypass surgery within the previous six months; (3) severe pulmonary disease; and, (4) serum creatinine over 3.0 mg/dl. In order to parallel endpoints employed in carotid stent trials, the in-hospital rate of MI, stroke, or death was calculated separately and as a combined endpoint

MI, stroke, or death occurred in 3.8% of all patients. When stratified by pre-procedural risk category, 19.4% of patients met the criteria for high-risk. Overall MI, stroke, or death occurred in 7.4% of the high-risk patient versus 2.9% of the "low-risk" patients. Individual endpoints of death (4.4% vs. 0.3%), stroke (3.5% vs. 1.7%) and MI (1.7% vs. 1.1%) were also higher in the high-risk patients.

McCrory et al. performed a structured review of hospital charts of 1160 randomly selected CEAs performed between 1987 and 1990 at 11 of 12 hospitals of the Academic Medical Centers Consortium.[37] After statistical analysis, significant predictors of adverse events in these cases were: (1) age >75 years; (2) presence of ipsilateral hemispheric instability; (3) severe hypertension; (4) CEA performed in preparation for bypass surgery; (5) evidence of internal carotid artery thrombus; and, (6) internal carotid artery stenosis near the carotid siphon. Combined in-hospital stroke, MI, or death was 6.9%. Other studies have demonstrated that high risk-patients enrolled in NASCET had significantly higher peri-operative adverse event rates compared to lower-risk patients.[38]

While it is clear that CEA is beneficial under the controlled and rigorously selected NASCET, ACAS, and ECST studies, adverse event rates surrounding this invasive surgical procedure for low and high-risk patients have led stroke prevention researchers to search for less invasive means of stroke prevention in patients with severe carotid artery disease. In addition, other techniques, including angioplasty, were considered for certain patients with difficult necks, postendarterectomy recurrent restenosis, and lesions secondary to radiotherapy.

Percutaneous Transluminal Angioplasty (PTA)

The objective of PTA is to improve flow through the diseased segment of a vessel so that vessel patency is increased and embolization is decreased. In most cases, a balloon dilation catheter with a non-elastic balloon is introduced into the vessel by the use of guidewires and guiding catheters, and inflated within the stenotic segment. Balloon angioplasty involves compression of atherosclerotic plaque, disruption and splitting of the plaque, intima, and media of the artery, and stretching of the adventitia of the arterial wall.[39]

With the development and use of balloon angioplasty for treatment of atherosclerotic and other vascular stenoses[40], PTA (with and without the placement of a stent) has become a widely used technique for dilating lesions of peripheral, renal, and coronary arteries.

PTA of the Carotid Artery

PTA of the carotid artery was first performed in the early 1980s and demonstrated that atherosclerotic lesion segments of the carotid artery could be dilated without necessarily provoking symptomatic cerebral artery thrombosis and embolism. However, limited research, consisting primarily of case reports, did not provide conclusive evidence about the safety and effectiveness of this procedure, and the risk of cerebral artery embolism and thrombosis (due to manipulation of ulcerated plaques during the PTA) were seen as unacceptably high.

In a review of the literature regarding carotid angioplasty, Becquemin et al. found several studies reporting only a few patients and a far smaller number of larger series describing angioplasty of various supra-aortic lesions (including those in the internal carotid artery).[41] The authors found an unacceptably high complication rate in the early reports of carotid angioplasty, and a lack of standard reporting guidelines in the later studies (including incomplete follow-up and lack of duplex scanning or angiographic data). They conclude that "it is difficult to draw any valid conclusions regarding the benefits of PTA of the carotid artery," but point out that "primary stenting may well be the optimal solution for carotid stenosis, thus avoiding plaque dislodgement, dissection, and arterial recoil."[42] In summary, the unreliable immediate results of balloon angioplasty and the exposed, potentially thrombotic, or occlusive treated segment post-procedure has made PTA of the carotid artery alone an unsuitable treatment for atherosclerotic carotid lesions.

With the refinements in endovascular surgery and the development of new wires, catheters, low-profile balloons, and stents, clinicians began investigating the use of vascular stents concurrent with PTA in the carotid arteries for the treatment of carotid stenosis. This procedure is distinctly different than PTA of the carotid artery alone. In general, the placement of a carotid stent concurrent with PTA is believed to result in improved lumen size and minimizes the risk of plaque embolization, residual stenosis, platelet adhesion or thrombosis by dilating the lumen of the vessel and covering the carotid plaque with the stent.

Summary of Carotid Angioplasty-Stenting Evidence

PTA and stenting for carotid stenosis has been considered in patients for whom CEA may be (1) excessively difficult; (2) technically unfeasible; (3) accompanied by increased morbidity due to stenotic lesions after prior CEA; and, (4) accompanied by increased morbidity and mortality due to severe coexisting disease. Other proposed advantages of PTA concurrent with stent placement compared to CEA are: (1) general anesthesia is not required; (2) cranial nerve palsies are infrequent sequelae; (3) simultaneous procedures can be done on carotid and coronary arteries; and, (4) distal lesions in the high cervical or intracranial internal carotid artery can be accessed.

Several protocol-based angioplasty-stent studies have been performed, and most centers performing this procedure have reported the results. One large multi-center prospective experience comes from the North American Cerebral Percutaneous Transluminal Angioplasty Register (NACPTAR).[43] Interim results were reported on 165 angioplasties in 147 symptomatic non-surgical patients. The average stenosis pre-PTA was 84%, post-PTA 37%. The 30-day combined rate of death and stroke from all causes was 9%.

Mathur et al. reported on 231 patients with >60% stenosis in the extracranial arteries treated with PTA and stenting at the University of Alabama at Birmingham between 1994 and 1997.[44] A total of 271 vessels were treated during 259 procedures. In this case series, the average patient was 69 years old. Twenty-two percent of patients had prior CEA surgery of the stented artery, and 60% of patients had symptomatic carotid stenosis. The authors report that 79% of arteries treated in this series would have been excluded by NASCET and ACAS criteria.

For the entire patient group, major strokes occurred in two patients (0.9%), and minor strokes occurred in 17 patients (7.4%). Two deaths were reported. On univariate analysis, increased age, lesion severity, and long and/or multiple lesions were associated with the risk of procedural stroke. The authors report that in the NASCET eligible sub-population of this study, the risk of any stroke and death was 2.7%.

Several small case series have been published regarding analyses of certain patient sub-populations receiving angioplasty and stenting. These include an analysis of the University of Alabama data for 26 patients with >60% stenosis of the extracranial carotid arteries treated with carotid stenting in the presence of contralateral carotid occlusion.[45] In this study, Mathur et al. reported a procedural success rate of 96%, with one minor stroke reported (3.6% complication rate) at six months.

Yadav et al. reported on 22 patients who had stenting and angioplasty of 25 carotid arteries for restenosis after CEA at one major medical center.[46] In this series, the average patients was 69 years old, 68% were male, and 100% were caucasion. Follow-up was available on only eight patients (mean length of follow-up, 8 months). No repeat angioplasties or CEAs were reported. The authors reported a complication rate of 4% per treated artery (1 peri-procedural stroke reported).

The Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS), a prospective, randomized, non-blinded, controlled trial enrolling patients in Europe, has reported preliminary results in abstract form.[47] To date, 251 patients have been randomized to angioplasty, and 253 patients have been randomized to CEA. The authors reported that PTA was carried out using balloon catheters with the adjunctive use of stents in 26% of the angioplasty group. They did not report specifics regarding why certain patients received stents in addition to PTA, nor did they describe in detail the design of this study. In this abstract, they reported no difference in 30-day disabling stroke or death rates between the two groups (6% each group). It is difficult to extrapolate useful information from the limited data published from this study, although the authors have reported on the rates of re-stenosis in the surgical and angioplasty group.[48]

The European CAST I Study was a nonrandomized multicenter trial that enrolled 99 patients in seven European surgical centers to evaluate endovascular treatment of internal carotid artery stenoses using the Palmaz stent.[49] Inclusion criteria required patients to be 65 years or older with symptomatic or asymptomatic stenoses >70% as defined by NASCET criteria. Major exclusion criteria included coagulation disorders, renal insufficiency, or embologenic cardiopathy. Fifty-eight percent of enrolled patients were defined as symtomatic, and 83% of the diagnosed lesions were new (8% were post-radiation stenoses and 9% were post-surgical restenoses).

Ninety-nine stents were implanted in 96 patients (three cases were abandoned for inability to access the artery or deploy the stent; these patients were successfully converted to surgery). The authors reported a 6% procedure-related complication rate, including one reversible internal carotid artery spasm, two dissections, one cervical hematoma, and two residual stenoses. No peri-operative death or MI was reported. During the 24-month follow-up (mean 13 months) there were no reported neurological events or procedurally related deaths. One asymptomatic occlusion and three asymptomatic, non-flow limiting restenoses were found within one year.

Roubin et al. followed 528 consecutive patients (604 hemispheres/arteries) undergoing carotid stenting by a single group of operators.[50] Clinical follow-up was available on 518 (99.6%) of the 520 patients who survived the peri-procedural period. They found a .6% fatal stroke rate and a 1% non-stroke death rate at 30 days. The overall 30-day stroke and death rate was 7.4%, and the authors report a significant decline in the 30-day minor stroke rate during the five year study period ($p<0.05$ for the trend). There were no differences in freedom from stroke between men and women and symptomatic and asymtomatic patients. The best predictor of stroke was age equal to or greater than 80.

The authors reported several limitations of this study, including the possibility of confounding factors and a difference (compared to other CEA trials) in the method of calculating stroke and long-term survival analyses in terms of all-cause deaths. Roubin et al. conclude that carotid stenting can be performed with an acceptable 30-day complication rate and that the high freedom from ipsilateral stroke at three years suggests that carotid stenting is durable and efficacious.

In a continuing series of updates, Wholey et al. reported that a review of the major centers performing carotid angioplasty-stenting yielded a combined minor and major stroke and procedure-related death rate of 4.77% for a combined population of 4,453 patients receiving a total of 4,865 endovascular carotid artery stent procedures.[51] Recently published data from this registry reported an overall minor stroke rate of 2.72%, a major stroke rate of 1.49%, and a mortality rate of 0.86%.[52]

Although there have been a small number of reports of carotid stenting trials that question the effectiveness of this procedure[53], the current body of literature suggests that carotid stenting may present a better therapeutic option for certain patients and potentially provide a reasonable alternative to surgical CEA. While several studies have shown that in selected patients, PTA concurrent with stenting may decrease or eliminate the carotid stenosis with peri-procedural complications comparable to or better than CEA, to date there have been no large, rigorously designed, well-controlled studies examining this procedure.

In 1998, The American Heart Association (AHA) issued an AHA Medical/ Scientific statement which noted that although "the techniques of carotid angioplasty and stenting are available… at this point, with few exceptions, use of carotid stenting should be limited to well-designed, well-controlled randomized studies with careful, dispassionate oversight. This will allow accurate comparison of a promising tool with the well-described, relatively safe gold standard of surgical carotid endarterectomy."[54] Other investigators have also concluded that while preliminary reports suggest that carotid stenting can be performed with acceptable 30-day complication rates, "whether carotid stenting is a reasonable alternative to CEA and thus should be compared directly depends on more definitive evidence."[55] In addition, a recent multi-disciplinary consensus panel of 17 individuals who have significant experience and interest in carotid stenting-angioplasty concluded that carotid angioplasty-stenting is currently appropriate treatment for patients at high-risk in experienced centers but not generally appropriate for patients at low-risk.[56] The panel also concluded that carotid angioplasty-stenting should not become widespread practice, but should await results of randomized trials.

HCFA Analysis

This decision considers whether carotid PTA, when performed solely for the purpose of dilation concurrent with carotid stent placement, should be considered reasonable and necessary, and therefore reimbursed by Medicare, when provided in an approved Category B IDE clinical trial. Future evaluation of other items or services for coverage under certain conditions will be evaluated on a case by case basis, under criteria similar, but not limited to, those discussed below, with any decision dependent on a thorough scientific evaluation of the specific issue.

Currently, there are no FDA approved stents for use in the carotid artery. However, as evidence regarding the effectiveness of stent placement in other vessels has advanced, and new technology and equipment specific to PTA and stenting of the carotid artery has developed[57], several large IDE studies have either been approved by the FDA or are in the approval process to investigate carotid artery stenting and its potential applications.[58] The stents being used in these trials have been designated Category B IDE devices by the FDA. In 1996, FDA issued a guidance document detailing suggestions for carotid stent IDE applications.[59]

The stated purpose of this guidance document is to "describe the format and content of an IDE application for carotid stenting." Because the FDA considers a stent in the carotid artery a significant risk device, legal and ethical considerations require that studies involving US patients be carried out under an IDE. This guidance document lays out the suggested components an IDE application involving carotid stenting should contain. These components include: 1) reports of prior investigations; 2) an overall clinical plan (including a brief description of study design, sample size, primary outcome measures, and principal results); 3) an investigational plan (including name and intended use of the device, objectives of this investigation, duration of the investigation, and number of patients involved); 4) manufacturing information (including information on the device manufacturing, materials, processing, packaging, storage, and installation information); 5) investigator agreement (including a sample of the sponsor's investigator agreement and the curiculum vitae of each principal investigator); 6) Institutional Review Board (IRB) information and informed consent form (including the name and address of the IRB chairman, a copy of the informed consent form, and the IRB study approval information); 7) sales information; and, 8) other information (including labeling information, environmental impact statement, and other required reporting documentation).

In Attachment C of this document (methodology suggestions) the FDA noted that "although there are no methodological requirements [for carotid stent IDE applications], the unique nature of carotid disease and the established safety and effectiveness of carotid endarterectomy suggested the inclusion of the following elements in carotid stent IDE applications." These elements include:

- Outcome measures and methodology; including peri-operative morbidity, ipsilateral stroke (major and minor) with actuarial reporting, and symptom resolution.
- The development of a multidisciplinary team including a physician skilled in neurology, a physician skilled in interventional neuroradiology, and a surgeon skilled in performing CEA.
- Study design information; including the possible necessity of a long-term, randomized concurrent-control trial (RCT) versus CEA to demonstrate the safety and effectiveness of carotid stenting.
- The development of a Data Safety and Monitoring Committee (DSMC), including an interventionalist, neurologist, vascular surgeon, and statistician independent of the sponsor and investigator of the trial. This DSMC should specify stopping rules for adverse outcome before the study begins.
- Qualification of the device.
- Qualification of the interventional team, including development of a rational approach to training, monitoring, and acceptance of each member of the multidisciplinary team.

Several Category B IDE trials received FDA approval and are currently enrolling patients. These include the NIH sponsored CREST trail, the SAPPHIRE trial, the Acculink for Revascularization of Carotids in High-Risk Patients (ARCHeR) trial, and the Stenting of High Risk Extracranial Lesions Trial with Emboli Removal (SHELTER) trial. All of these trials have extensive protocols addressing the methodological issues discussed above. In particular, these include, but are not limited to, study objective and design statements, strict subject selection (inclusion/exclusion) guidelines, informed consent rules, safety monitoring rules established by independent DSMCs, and study procedure descriptions.

Category B IDE trials currently in the approval process include the Evaluation of the Medtronic AVE Self-Expanding Carotid Stent System with Distal Protection in the Treatment of Carotid Stenosis (MAVErIC) trial, and the Carotid Revascularization with Endareterectomy or Stenting Systems (CARESS) trial.

While the study designs differ and the patient populations under investigation vary between studies, primary endpoints, at a minimum, include major adverse event rates (any stroke, death, or myocardial infarction during the 30-day peri-procedural period) and major adverse events and/or stroke ipsilateral to the procedure thereafter.

In addressing the issue of coverage for PTA of the carotid artery concurrent with stenting in an approved Category B IDE trial, the following questions arise:

- Does enough information exist about carotid angioplasty-stenting for HCFA to determine that some basic safety and efficacy issues have been resolved and therefore, the service can be considered reasonable and necessary under particular conditions?
- Have these trials undergone appropriate scientific review? Are the proposed trial designs sufficient to answer the clinical questions pertinent to Medicare beneficiaries?
- Without data from these trials, would the evidence regarding the effectiveness of angioplasty-stenting versus CEA be available for certain high and low-risk patients?

As summarized earlier in this memo, stroke causes substantial morbidity and mortality for Medicare patients and accounts for substantial numbers of hospitalizations and health care costs. Stroke is recognized as one of the six clinical priority areas in the Health Care Quality Improvement Program (HCQIP) launched by the HCFA in 1992, and CEA is performed frequently in Medicare patients with severe carotid stenosis.

As a result of the importance of stroke risk reduction for our beneficiaries, we recognize that making available new, effective therapies aimed at addressing this problem are critically important, and support of trials investigating these therapies may help aid this process. Therefore, we feel that the current and proposed carotid angioplasty-stenting trials are of significant importance to the Medicare population.

HCFA recognizes that these Category B IDE clinical trials are research studies designed to evaluate the safety and effectiveness of a new technology, and their findings may be crucial to potentially improving clinical practice. Furthermore, we believe that the oversight provided by institutional IRBs, strict adherence to study protocols, study conduct rules established by DSMCs, and sponsor/investigator qualification of the interventional teams, differentiate the performance of carotid angioplasty-stenting in these trials from that performed elswhere that do not possess these safeguards, and provides a reasonable assurance of safety. We understand that the results from these trials may answer a clinical question which may advance the treatment of carotid artery disease and stroke prevention. We recognize that not all these trials are randomized, and that the target populations differ. However, well-designed observational studies, implemented concurrently with randomized trials, may capture certain patients "excluded" from randomized designs, and may help strengthen the available evidence about a therapeutic modality for certain patient sub-groups. We believe the data from such studies will help us better understand the effectiveness of carotid stenting and also which high-risk patients may benefit most from this procedure. Therefore, it is our intention to include all approved Category B IDE trials in this policy.

After a complete review of the scientific and clinical evidence regarding carotid angioplasty-stenting, it is clear that PTA concurrent with stent placement is a different procedure than stand-alone PTA of the carotid artery, the procedure that was the basis for the previous national noncoverage policy. We have determined that although a body of evidence (primarily case series and single-center experiences) has been published and suggests a potential benefit to some patients, there is not sufficient information to: (1) predict the effect of generalized use of carotid stenting; (2) to evaluate the long-term outcomes of this therapy; and, (3) to determine the appropriate patient groups that may benefit. We do not believe a national coverage policy without restrictions is appropriate at this time for this procedure. However, we do believe that the available evidence regarding carotid stenting concurrent with angioplasty, and the FDA’s willingness to approve Category B IDE trials involving carotid stents, are sufficient to allow us to provide beneficiaries with limited access to this promising technology. Therefore, we believe that there is sufficient evidence to indicate that carotid angioplasty, when performed concurrent with carotid stenting, is a reasonable and necessary service when provided in a Category B IDE trial.

Although Medicare coverage for this procedure is limited to its provision in an approved Category B IDE trial, HCFA will regularly monitor the results of these trials and continue its dialogue with the manufacturers of these devices and the researchers and clinicians involved in this area. By extending coverage to these trials, we expect organizations to provide HCFA and the scientific community with their results in a timely fashion, and we will evaluate their findings to determine if the evidence is sufficient to expand the national coverage policy related to these services outside of clinical trials.

Conclusion

Medicare will cover PTA of the carotid artery concurrent with stent placement in clinical trials that receive a Category B IDE designation from the FDA. Carotid angioplasty, when provided solely for the purpose of dilation concurrent with carotid stent placement, is considered to be a reasonable and necessary service only when provided in the context of such a Category B IDE clinical trial, and therefore is considered a covered service for the purposes of these trials. Although the carotid stent used in this procedure is presently under evaluation as a Category B investigational device, the PTA used to place the stent (and all services related to this procedure) are considered covered services for Medicare beneficiaries participating in such trials.

Performance of PTA in the carotid artery when used to treat obstructive lesions outside of a qualifying Category B IDE clinical trial remains a noncovered service, and PTA of the vertebral and cerebral arteries remains noncovered.

Decision

Amend CIM 50-32 to state:

PTA is not covered to treat obstructive lesions of the carotid artery except in the following circumstance:

Medicare will cover PTA of the carotid artery concurrent with stent placement in clinical trials that receive a Category B IDE designation from the FDA. PTA of the carotid artery, when provided solely for the purpose of dilation concurrent with carotid stent placement, is considered to be a reasonable and necessary service only when provided in the context of such a clinical trial, and therefore is considered a covered service for the purposes of these trials. Although the carotid stent used in this procedure is presently under evaluation as a Category B investigational device, the PTA used to place the stent (and all services related to this procedure) are considered covered services.

Performance of PTA in the carotid artery when used to treat obstructive lesions outside of an approved Category B IDE clinical trial remains a noncovered service.

PTA of the of the vertebral and cerebral arteries remains noncovered.

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1 See Medicare Carrier Manual, section 2300.1.

2 See Wiggli U, Gratzl O. Transluminal angioplasty of stenotic carotid arteries: case reports and protocol; Bockenheimer SM, Mathias K. Percutaneous transluminal angioplasty in arteriosclerotic internal carotid artery stenosis; and, Vitek JJ. Percutaneous transluminal angioplasty of the external carotid artery. AJNR 1983;4.

3 PHS (OHTA) Assessment, Percutaneous transluminal angioplasty for obstructive lesions of the aortic arch vessels, 1984.

4 See Coverage Issues Manual §50-32.

5 See TAC minutes, February 1993.

6 See TAC minutes, June 1993.

7 See 42 CFR §§405.20 - 405.215 and §411.15.

8 See TAC minutes, February 1997.

9 See Medicare's policy at section 2300.1 of the Medicare Carrier Manual, which prohibits payment for items and services related to the provision of noncovered services.

10 The Carotid Revascularization Endarterectomy-Stenting Trial (CREST), is a randomized, controlled, clinical trial in symptomatic patients with extracranial carotid stenosis >50% (as measured by angiography) comparing the efficacy of carotid artery stenting and CEA in preventing stroke, myocardial infarction, and death in the peri-procedural period and ipsilateral stroke over the follow-up period (extending up to 4 years). This study will enroll approximately 2500 patients.

11 The Stenting and Angioplasty with Protection in Patients at High-Risk for Endarterectomy Trial (SAPPHIRE) is a randomized, prospective, multi-center parallel stent and CEA registry comparing carotid-angioplasty stenting versus CEA in high-risk surgical and medical patients.

12 www.hcfa.gov/coverage

13 Goldman et al. 2000.

14 American Stroke Association 2000 - Impact of Stroke.

15 American Stroke Association 2000. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study (ACAS) 1995.

16 Goldman L, et al. 2000.

17 Chaturvedi S 1999.

18 ACAS 1995.

19 Ibid.

20 Tu J, et al. 1998.

21 These include the increasing evidence of the effectiveness of risk-factor management and the efficacy of antiplatelet drugs in preventing stroke.

22 Barnett H, et al. 1998.

23 European Carotid Surgery Trialists Collaborative Group (ECST) 1991.

24 ECST 1991.

25 NASCET Collaborators 1991.

26 Qualifying trial centers had to have a complication rate of less than 6% for stroke and death within 30 days of CEA for at least 50 procedures performed within the two years previous to the trial.

27 The study was terminated early in patients with 70-99% stenosis after an interim analysis demonstrated these results.

28 Barnett H, et al. 1998.

29 Mayberg M, et al. 1991. This study was terminated early after the results of NASCET and ECST were reported.

30 Qualifying centers had to have a stroke morbidity and mortality rate of less than 6% for all prior CEAs performed.

31 ACAS 1995.

32 Hobson R, et al. 1993.

33 Bettmann M, et al. 1998.

34 Wennberg D. et al. 1998.

35 Chatvurdi S 1999. Also Chassin M 1998.

36 Ouriel K, et al. 1999.

37 McCrory D, et al. 1993.

38 Gasecki A, et al. 1995.

39 American College of Physicians 1983.

40 Gruntzig's development of a "flexible," double lumen, balloon-dilating catheter permitted extension of the technique from the iliofemoral vessels to previously inaccesible sites such as coronary and renal arteries. See Gruntzig A, et al. 1974.

41 Becquemin et al. 1996.

42 Ibid.

43 The NACPTAR investigators 1995.

44 Mathur A, et al. Circulation 1998.

45 Mathur A, et al. American Journal of Cardiology 1998.

46 Yadav J, et al. 1996.

47 Brown M 1999.

48 McCabe D et al. 1999.

49 Bergeron P, et al. 1999.

50 Roubin G, et al. 2001.

51 Wholey M, et al. 1999.

52 Wholey M, et al. 2000.

53 Naylor A, et al. 2000. Alberts M 2001.

54 Bettmann M, et al. 1998.

55 Roubin G, et al. 2001.

56 Veith F, et al. 2001.

57 These include carotid artery specific stents and delivery systems, as well as mechanical anti-embolic devices which will limit macroemboli from reaching the brain either by complete occlusion of the distal cerebral bed or by filtering the outflow from the stent deployment site.

58 An approved IDE permits a device to be shipped lawfully for the purpose of conducting investigations of the device without complying with special controls or having marketing clearance from FDA.

59 Carotid stent - suggestions for content of submissions to the Food and Drug Administration in Support of Investigational Device Exemption (IDE) applications. US Department of Health and Human Services. Public Health Service, Food and Drug Administration, Center for Devices and Radiological Health, October 26, 1996.

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